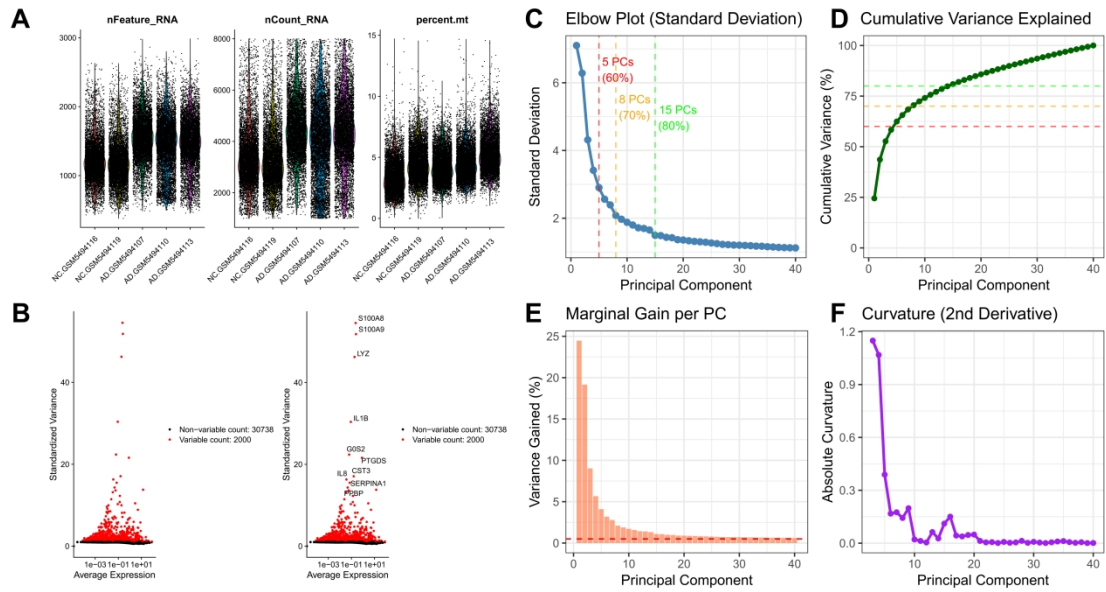
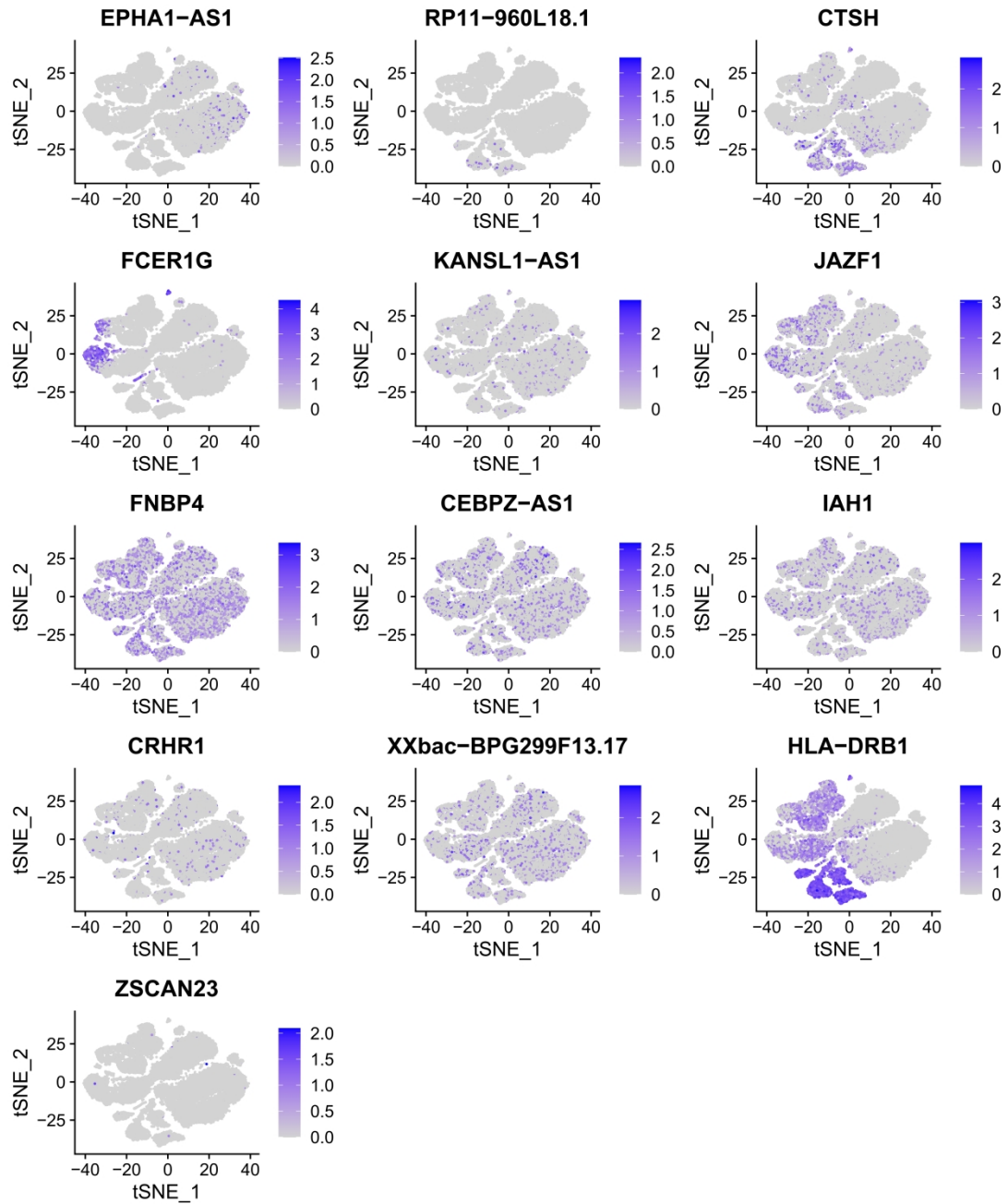




Supplementary Figure 1. Quality control and preprocessing of scRNA-seq data for analysis.

(A) Violin plots displaying quality control metrics for each sample, including nCount_RNA (total number of RNA molecules), nFeature_RNA (number of genes detected per cell), and percent.mt (percentage of mitochondrial gene expression). (B) Variance plot identifying the top 2,000 highly variable genes selected for downstream analysis. (C-F) Principal component standard deviation plots used to determine the number of informative components retained for clustering.



Supplementary Figure 2. tSNE feature plots illustrating cell-type-specific expression patterns of prioritized eGenes.

Feature plots visualize the spatial expression patterns of genetically prioritized genes across immune cell clusters. These distributions illustrate subset-enriched transcriptional activity.

Gene Symble	Gene ID	Cell ID	PP.H0	PP.H1	PP.H2	PP.H3	PP.H4
EPHA1-AS1	ENSG00000229153	Mono C	0.00%	0.00%	0.00%	0.06%	99.94%
RP11-960L18.1	ENSG00000261218	B IN	0.00%	0.00%	0.00%	0.32%	99.68%
CTSH	ENSG00000103811	Mono NC	0.00%	0.16%	0.00%	0.22%	99.62%
CTSH	ENSG00000103811	CD4 NC	0.00%	0.21%	0.00%	0.32%	99.48%
KANSL1-AS1	ENSG00000214401	Mono C	0.00%	0.01%	0.00%	0.65%	99.34%
KANSL1-AS1	ENSG00000214401	NKR	0.00%	0.01%	0.00%	0.65%	99.34%
FCER1G	ENSG00000158869	DC	0.00%	0.00%	0.00%	0.73%	99.27%
CTSH	ENSG00000103811	Mono C	0.00%	0.31%	0.00%	0.53%	99.15%
FCER1G	ENSG00000158869	Mono C	0.00%	0.00%	0.00%	0.92%	99.08%
FCER1G	ENSG00000158869	Mono NC	0.00%	0.00%	0.00%	1.08%	98.91%
CTSH	ENSG00000103811	B MEM	0.00%	0.42%	0.00%	0.75%	98.83%
CTSH	ENSG00000103811	DC	0.00%	0.45%	0.00%	0.82%	98.72%
JAZF1	ENSG00000153814	CD4 NC	0.00%	0.01%	0.00%	1.38%	98.61%
KANSL1-AS1	ENSG00000214401	B MEM	0.00%	0.00%	0.00%	1.58%	98.42%
FNBP4	ENSG00000109920	B MEM	0.00%	0.00%	0.00%	1.98%	98.01%
CEBPZ-AS1	ENSG00000218739	CD8 ET	0.00%	0.73%	0.00%	3.92%	95.34%
IAH1	ENSG00000134330	CD4 ET	0.00%	0.06%	0.01%	5.71%	94.21%
EPHA1-AS1	ENSG00000229153	Mono NC	0.00%	0.00%	0.00%	8.83%	91.17%
KANSL1-AS1	ENSG00000214401	CD4 ET	0.00%	0.00%	0.00%	10.46%	89.53%
CRHR1	ENSG00000120088	CD8 NC	0.00%	0.20%	0.00%	11.07%	88.73%
XXbac-BPG299F13.17	ENSG00000272501	Plasma	0.00%	0.31%	0.00%	11.97%	87.73%
KANSL1-AS1	ENSG00000214401	CD4 NC	0.00%	0.00%	0.00%	12.52%	87.47%
KANSL1-AS1	ENSG00000214401	B IN	0.00%	0.00%	0.00%	12.66%	87.33%
KANSL1-AS1	ENSG00000214401	NK	0.00%	0.00%	0.00%	12.81%	87.18%
KANSL1-AS1	ENSG00000214401	CD8 ET	0.00%	0.00%	0.00%	13.94%	86.06%

HLA-DQA2	ENSG00000237541	Plasma	0.00%	0.00%	0.00%	15.00%	85.00%
ZSCAN23	ENSG00000187987	CD4 NC	0.00%	0.87%	0.00%	16.00%	83.13%
KANSL1-AS1	ENSG00000214401	CD8 S100B	0.00%	0.00%	0.00%	20.01%	79.98%
HLA-DQA1	ENSG00000196735	Mono NC	0.00%	0.00%	0.00%	30.58%	69.42%
KANSL1-AS1	ENSG00000214401	CD8 NC	0.00%	0.01%	0.00%	33.59%	66.40%
CRHR1	ENSG00000120088	CD4 NC	0.00%	0.01%	0.00%	35.82%	64.17%
XXbac-BPG181B23.7	ENSG00000272221	Mono NC	0.00%	3.71%	0.00%	33.11%	63.17%
RP11-798G7.5	ENSG00000131484	CD4 NC	0.00%	0.00%	0.00%	39.23%	60.77%
LRRC37A2	ENSG00000238083	CD8 NC	0.00%	0.00%	0.00%	39.65%	60.35%
LRRC37A2	ENSG00000238083	NK	0.00%	0.00%	0.00%	39.87%	60.12%
KANSL1-AS1	ENSG00000214401	DC	0.00%	0.00%	0.00%	42.90%	57.09%
RP11-669E14.6	ENSG00000262372	CD8 ET	0.00%	0.00%	0.00%	43.65%	56.34%
RP11-669E14.6	ENSG00000262372	CD8 NC	0.00%	0.00%	0.00%	53.28%	46.72%
FGFRL1	ENSG00000127418	CD4 ET	0.00%	0.06%	0.00%	62.80%	37.14%
IDUA	ENSG00000127415	CD4 NC	0.00%	0.06%	0.03%	65.10%	34.80%
ITPR3	ENSG00000096433	Plasma	0.00%	0.00%	0.02%	94.02%	5.96%
HLA-DQA1	ENSG00000196735	NKR	0.00%	0.00%	0.00%	96.06%	3.94%
RPS27L	ENSG00000185088	CD4 NC	0.00%	0.00%	0.33%	98.92%	0.74%
LAMTOR4	ENSG00000188186	CD4 ET	0.00%	0.00%	0.21%	99.13%	0.66%
VARS2	ENSG00000137411	DC	0.00%	59.43%	0.00%	40.02%	0.56%
GATS	ENSG00000160844	B IN	0.00%	0.00%	0.00%	99.77%	0.23%
HCG25	ENSG00000232940	CD8 ET	0.00%	0.00%	0.00%	99.79%	0.21%
ZBTB22	ENSG00000236104	NKR	0.00%	0.00%	0.00%	99.90%	0.10%
BIN1	ENSG00000136717	NKR	0.00%	0.00%	0.00%	99.96%	0.04%
BIN1	ENSG00000136717	B MEM	0.00%	0.00%	0.01%	99.98%	0.01%
BIN1	ENSG00000136717	CD8 S100B	0.00%	0.00%	0.00%	100.00%	0.00%

HLA-DRB5	ENSG00000198502	CD4 SOX4	0.00%	0.00%	0.02%	99.98%	0.00%
HLA-DRB1	ENSG00000196126	Mono NC	0.00%	0.00%	0.01%	99.99%	0.00%
CNN2	ENSG00000064666	CD8 ET	0.00%	0.00%	0.00%	100.00%	0.00%
CNN2	ENSG00000064666	CD8 NC	0.00%	0.00%	0.00%	100.00%	0.00%
EPHX2	ENSG00000120915	CD8 NC	0.00%	0.00%	0.00%	100.00%	0.00%
HLA-DRB5	ENSG00000198502	CD4 NC	0.00%	0.00%	0.00%	100.00%	0.00%
CNN2	ENSG00000064666	CD4 ET	0.00%	0.00%	0.00%	100.00%	0.00%
BIN1	ENSG00000136717	CD4 ET	0.00%	0.00%	0.00%	100.00%	0.00%
EPHX2	ENSG00000120915	CD4 NC	0.00%	0.00%	0.00%	100.00%	0.00%
AC092301.3	ENSG00000269148	CD8 NC	0.00%	0.00%	0.00%	100.00%	0.00%
BIN1	ENSG00000136717	CD8 NC	0.00%	0.00%	0.00%	100.00%	0.00%
BIN1	ENSG00000136717	CD8 ET	0.00%	0.00%	0.00%	100.00%	0.00%
BIN1	ENSG00000136717	NK	0.00%	0.00%	0.00%	100.00%	0.00%
BIN1	ENSG00000136717	CD4 NC	0.00%	0.00%	0.00%	100.00%	0.00%

Supplementary Table 1. Bayesian colocalization results for eGenes associated with AD.

Abbreviations: Plasma, plasma cells; B IN, immature/naïve B cells; B MEM, memory B cells; CD4 NC, naïve/central memory CD4⁺ T cells; CD4 ET, effector/central memory CD4⁺ T cells; CD4 SOX4, SOX4-positive CD4⁺ T cells; CD8 NC, naïve/central memory CD8⁺ T cells; CD8 ET, effector/central memory CD8⁺ T cells; CD8 S100B, S100B-positive CD8⁺ T cells; NK, natural killer cells; NKR, natural killer-recruiting cells; Mono C, classical monocytes; Mono NC, non-classical monocytes; DC, dendritic cells.

Gene Symble	Gene ID	Cell type	Method	nSNP	Beta	SE	P-value	Bonferroni P-value	OR_95CI
KANSL1-AS1	ENSG00000214401	B N	Wald ratio	1	-0.057	0.010	5.43E-09	6.52E-08	0.944 (0.926–0.963)
RP11-960L18.1	ENSG00000261218	B N	Wald ratio	1	0.086	0.012	1.98E-12	2.38E-11	1.090 (1.064–1.117)
JAZF1	ENSG00000153814	CD4 N	Wald ratio	1	-0.034	0.012	5.07E-03	6.09E-02	0.967 (0.944–0.990)
KANSL1-AS1	ENSG00000214401	CD4 N	Wald ratio	1	-0.051	0.009	5.43E-09	6.52E-08	0.951 (0.935–0.967)
CTSH	ENSG00000103811	CD4 N	Wald ratio	1	-0.001	0.016	9.46E-01	1.00E+00	0.999 (0.968–1.031)
CTSH	ENSG00000103811	Mono C	Wald ratio	1	0.066	0.014	1.75E-06	2.10E-05	1.068 (1.040–1.098)
EPHA1-AS1	ENSG00000229153	Mono C	Wald ratio	1	-0.046	0.007	8.03E-11	9.64E-10	0.955 (0.942–0.968)
FCER1G	ENSG00000158869	Mono C	Wald ratio	1	-0.090	0.016	1.46E-08	1.75E-07	0.914 (0.886–0.943)
KANSL1-AS1	ENSG00000214401	Mono C	Wald ratio	1	-0.049	0.008	5.43E-09	6.52E-08	0.952 (0.937–0.968)
CTSH	ENSG00000103811	Mono NC	Wald ratio	1	0.058	0.012	1.21E-06	1.45E-05	1.059 (1.035–1.084)
EPHA1-AS1	ENSG00000229153	Mono NC	Wald ratio	1	-0.048	0.007	8.03E-11	9.64E-10	0.953 (0.940–0.967)
KANSL1-AS1	ENSG00000214401	NK	Wald ratio	1	-0.051	0.009	5.43E-09	6.52E-08	0.951 (0.935–0.967)

Supplementary Table 2. Replication of prioritized immune cell-specific eGenes in the DICE sc-eQTL cohort using MR analysis.

Abbreviations: B N, naïve B cells; CD4 N, naïve CD4⁺ T cells; CD8 N, naïve CD8⁺ T cells; Mono C, classical monocytes; Mono NC, non-classical monocytes; NK, natural killer cells.

Gene	Cell type	Log2 FC	Average expression in AD	Average expression in NC	P-value	FDR P-value
FCER1G	Mono C	-0.285	0.945	0.973	1.71E-03	6.40E-03
CTSH	Mono C	-0.512	0.547	0.649	1.16E-02	2.99E-02
EPHA1-AS1	Mono C	-1.099	0.000	0.007	3.56E-01	4.93E-01
KANSL1-AS1	Mono C	-0.341	0.039	0.054	5.77E-01	6.58E-01
RP11-960L18.1	B IN	0.970	0.072	0.028	2.24E-04	1.34E-03
KANSL1-AS1	B IN	0.146	0.045	0.033	2.55E-01	4.18E-01
IAH1	CD4 T	0.282	0.187	0.123	1.63E-20	2.93E-19
CTSH	CD4 T	0.469	0.069	0.041	3.77E-13	3.39E-12
KANSL1-AS1	CD4 T	-0.118	0.079	0.064	1.78E-03	6.40E-03
JAZF1	CD4 T	-0.302	0.074	0.070	7.06E-01	7.47E-01
ZSCAN23	CD4 T	-0.134	0.001	0.001	9.25E-01	9.25E-01
CTSH	B MEM	-0.211	0.403	0.439	4.11E-03	1.23E-02
FNBP4	B MEM	0.266	0.490	0.435	2.45E-02	5.51E-02
KANSL1-AS1	B MEM	-0.146	0.042	0.046	5.85E-01	6.58E-01
KANSL1-AS1	CD8 T	-0.110	0.068	0.058	1.44E-01	2.88E-01
CRHR1	CD8 T	0.068	0.025	0.020	2.08E-01	3.74E-01
CEBPZ-AS1	CD8 T	-0.326	0.170	0.166	3.24E-01	4.86E-01
KANSL1-AS1	NK	-0.234	0.062	0.056	5.57E-01	6.58E-01

Supplementary Table 3. Exploratory differential expression results for prioritized eGenes across peripheral blood immune cell populations.

Abbreviations: CD4 T, CD4⁺ T cells; CD8 T, CD8⁺ T cells; B IN, immature/naïve B cells; B MEM, memory B cells; Mono C, classical monocytes; NK, natural killer cells.

Gene	Immune cell-type and MR direction	PP.H4 (%)	DICE	scRNA-seq
KANSL1-AS1	↓ Mono C, NKR, B MEM, CD4 ET, CD4 NC, B IN, NK, CD8 ET	86.06–99.34	R	C: CD4 T
CTSH	↑ Mono NC, Mono C, B MEM, DC; ↓ CD4 NC	98.72–99.62	PR	DE: CD4 T, Mono C, B MEM; E
FCER1G	↓ DC, Mono C, Mono NC	98.91–99.27	R	C: Mono C; E
EPHA1-AS1	↓ Mono C, Mono NC	91.17–99.94	R	—
RP11-960L18.1	↑ B IN	99.68	R	C: B IN
JAZF1	↓ CD4 NC	98.61	NT	—
FNBP4	↓ B MEM	98.01	NT	—
CEBPZ-AS1	↓ CD8 ET	95.34	NT	—
IAH1	↑ CD4 ET	94.21	NT	C: CD4 T
CRHR1	↑ CD8 NC	88.73	NT	—
XXbac-BPG299F13.17	↑ Plasma	87.73	NT	—
HLA-DQA2	↓ Plasma	85.00	NT	—
ZSCAN23	↓ CD4 NC	83.13	NT	—

Supplementary Table 4. Integrated evidence for strongly colocalized immune cell-specific eGenes associated with AD.

Notes:

1. ↑ and ↓ indicate that genetically predicted higher expression was associated with increased and decreased AD risk, respectively.
2. Strong colocalization was defined as PP.H4 > 80%.
3. DICE status: R, replicated; PR, partially replicated across tested cell types; NT, not testable because a matched cell type or eligible instrument was unavailable; NR, not explicitly reported in the main text.
4. scRNA-seq support: C, FDR-significant differential expression concordant with the genetic analysis; DE, FDR-significant differential expression; E, cell-type-enriched expression; —, no specific supporting signal identified.

Abbreviations: B IN, immature/naïve B cells; B MEM, memory B cells; CD4 NC, naïve/central memory CD4⁺ T cells; CD4 ET, effector/central memory CD4⁺ T cells; CD8 NC, naïve/central memory CD8⁺ T cells; CD8 ET, effector/central memory CD8⁺ T cells; Mono C, classical monocytes; Mono NC, non-classical monocytes; NK, natural killer cells; NKR, natural killer-recruiting cells; DC, dendritic cell.

Term	P-value	Odds ratio	Combined score	BBB permeant	Genes
fucose TTD 00008125	7.18E-03	167.86	828.65	No	FCER1G
alpha-D-Mannose TTD 00001913	1.08E-02	109.70	497.26	No	FCER1G
asparagine BOSS	1.63E-02	71.26	293.40	No	CTSH
NSC94017 CTD 00005320	3.31E-02	34.27	116.77	No	CRHR1
Bexarotene CTD 00003225	3.58E-02	31.59	105.16	No	CTSH
chloroquine BOSS	3.85E-02	29.30	95.40	Yes	CTSH
Cianidanol CTD 00005600	4.44E-02	7.34	22.87	No	CRHR1; JAZF1

Supplementary Table 5. All candidate drugs from DSigDB predicted to target prioritized AD-associated eGenes.

Drug	Target	Structure ID	Pocket definition	Grid center (Å)	Grid points	Spacing (Å)	Docking runs	Predicted Ki	BBB permeant	Binding energy (kcal/mol)
Bexarotene	CTSH	6CZK	Global blind docking	16.010, 51.491, 42.770	$96 \times 108 \times 94$	0.575	50	730.78 nM	No	-8.37
Chloroquine	CTSH	6CZK	Global blind docking	14.666, 50.993, 42.770	$98 \times 122 \times 98$	0.481	50	107.66 μ M	Yes	-5.41
NSC94017	CRHR1	3EHS	Global blind docking	111.742, 140.418, 134.190	$58 \times 102 \times 126$	0.792	50	118.73 μ M	No	-5.36
Cianidanol	JAZF1	AF-Q86VZ6-F1-model_v6	Global blind docking	0.326, 21.511, -14.680	$100 \times 96 \times 126$	0.836	50	329.63 μ M	No	-5.34
Cianidanol	CRHR1	3EHS	Global blind docking	112.184, 140.203, 134.131	$56 \times 102 \times 126$	0.792	50	180.05 μ M	No	-5.11
Asparagine	CTSH	6CZK	Global blind docking	16.010, 51.491, 42.770	$96 \times 108 \times 94$	0.575	50	1.01 mM	No	-4.09
Fucose	FCER1G	7Q5T	Global blind docking	-15.287, -7.629, 22.289	$100 \times 76 \times 126$	0.742	50	6.85 mM	No	-2.95
Alpha-D-Mannose	FCER1G	7Q5T	Global blind docking	-15.287, -7.629, 22.289	$100 \times 76 \times 126$	0.742	50	22.21 mM	No	-2.26

Supplementary Table 6. Comprehensive details of the molecular docking simulation.

Trait	Full Name	Sample Size	Link
AD	Alzheimer's disease	487,511	https://www.ebi.ac.uk/gwas/studies/GCST90027158
CD4 NC	CD4 Naïve/Central memory T cell	982	https://onek1k.org
CD4 ET	CD4 Effector memory/TEMRA	982	https://onek1k.org
CD4 SOX4	CD4 SOX4 T cell	857	https://onek1k.org
CD8 NC	CD8 Naïve/Central memory T cell	982	https://onek1k.org
CD8 ET	CD8 Effector memory	982	https://onek1k.org
CD8 S100B	CD8 S100B T cell	981	https://onek1k.org
B Mem	Memory B Cell	982	https://onek1k.org
B IN	Naïve/Immature B Cell	982	https://onek1k.org
Mono NC	Non-classic Monocyte	932	https://onek1k.org
Mono C	Classic Monocyte	969	https://onek1k.org
NK R	NK recruiting Cell	967	https://onek1k.org
NK	Natural killer Cell	928	https://onek1k.org
DC	Dendritic Cell	968	https://onek1k.org
Plasma	Plasma Cell	643	https://onek1k.org

Supplementary Table 7. Brief summary of the GWAS datasets analyzed in this study.

Supplementary Data 1. MR results for AD eGenes across immune cell types.

Supplementary Data 2. IVs information used for MR analysis.